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|   | n PTO-<br>V 10-96  | 1390-MOD U. S.   | Department of Commerce Patent and Trademark Office     | ATTORNEY'S DOCKET NUMBER                    |  |  |  |  |  |  |  |  |  |
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| (KE   | V 10-90  |  | 33378A   |   |  |  |  |  |  |  |  |  |  |
|   |  | TRANSMITTAL LETTER TO T  | U.S. APPLICATION NO. (If known, see 37 CFR 1.5)        |   |  |  |  |  |  |  |  |  |  |
|   |  | DESIGNATED/ELECTED O   | 10/573208  |   |  |  |  |  |  |  |  |  |  |
| CONCERNING A FILING UNDER 35 U.S.C. 371                             |  |  |  |   |  |  |  |  |  |  |  |  |  |
|   |  | NATIONAL APPLICATION NO.<br>P2004/010688   | INTERNATIONAL FILING DATE 23 September 2004 (23.09.04) | PRIORITY DATE CLAIMED                       |  |  |  |  |  |  |  |  |  |
|   |  | OF INVENTION   | 23 September 2004 (23.09.04)                           |   |  |  |  |  |  |  |  |  |  |
| 1,4   | 1,4-DISUBSTITUTED ISOQUINILONE DERIVATIVES AS RAF-KINASE INHIBITORS USEFUL FOR THE TREATMEN  |  |  |   |  |  |  |  |  |  |  |  |  |
| OF PROLIFERATIVE DISEASES APPLICANT(S) FOR DO/EO/US                 |  |  |  |   |  |  |  |  |  |  |  |  |  |
|   |  | JANT(S) FOR DO/EO/US<br>HA ANNE FINK   |  |   |  |  |  |  |  |  |  |  |  |
| 1.<br>2.<br>3.  | <ol> <li>This is a SECOND or SUBSEQUENT submission of items concerning a filing under 35 U.S.C. 371.</li> <li>This express request to begin national examination procedures (35 U.S.C. 371(f)) at any time rather than delay examination until the expiration of the applicable time limit set in 35 U.S.C. 371(b) and PCT Articles 22 and 39(1).</li> </ol> |  |  |   |  |  |  |  |  |  |  |  |  |
| ₽.  | Ц  | date.  | linary Examination was made by the 19t                 | th month from the earliest claimed priority |  |  |  |  |  |  |  |  |  |
| 5.  | $\boxtimes$  | A copy of the International Application as filed (35 U.S.C. 371(c)(2))  a.  is transmitted herewith (required only if not transmitted by the International Bureau).  b.  has been transmitted by the International Bureau. (See Form PCT/IB/308)   |  |   |  |  |  |  |  |  |  |  |  |
| 6.  |  | c. is not required, as the application was filed in the United States Receiving Office (RO/US).  A translation of the International Application into English (35 U.S.C. 371(c)(2)).  Amendments to the claims of the International Application under PCT Article 19 (35 U.S.C.371(c)(3))   |  |   |  |  |  |  |  |  |  |  |  |
| 7.  | $\boxtimes$  |  |  |   |  |  |  |  |  |  |  |  |  |
|   |  | a. \( \text{are transmitted herewith (required only if not transmitted by the International Bureau).} \) b. \( \text{have been transmitted by the International Bureau.} \) c. \( \text{have not been made; however, the time limit for making such amendments has NOT expired.} \) d. \( \text{have not been made and will not be made.} \) |  |   |  |  |  |  |  |  |  |  |  |
| 8.  |  | A translation of the amendments to the cl  | aims under PCT Article 19 (35 U.S.C. 3                 | 71 (c)(3)).                                 |  |  |  |  |  |  |  |  |  |
| 9.<br>10.   | Ш  | An executed Declaration and Power of Attorney (original or copy) (35 U.S.C. 371(c)(4)).  A translation of the annexes to the International Preliminary Examination Report under PCT Article 36 (35 U.S.C. 371(c)(5)).  |  |   |  |  |  |  |  |  |  |  |  |
| Items 11. to 16. below concern document(s) or information included. |  |  |  |   |  |  |  |  |  |  |  |  |  |
| 11.   |  | An Information Disclosure Statement und  | ler 37 CFR 1.97 and 1.98.                              |   |  |  |  |  |  |  |  |  |  |
| 12.   |  | An assignment document for recording. A separate cover sheet in compliance with 37 CFR 3.28 and 3.31 is included.  |  |   |  |  |  |  |  |  |  |  |  |
| 13.   |  | A FIRST preliminary amendment. A SECOND or SUBSEQUENT preliminar   | y amendment.   |   |  |  |  |  |  |  |  |  |  |
| 14.   | $\boxtimes$  | An Application Data Sheet under 37 CFR 1.76.   |  |   |  |  |  |  |  |  |  |  |  |
| 15.   |  | A substitute specification.  |  |   |  |  |  |  |  |  |  |  |  |
| 16.   |  | A change of power of attorney and/or address letter.   |  |   |  |  |  |  |  |  |  |  |  |
| 17.   | _  | A computer-readable form of the sequence listing in accordance with PCT Rule 13ter.2 and 37 CFR 1.821-1.825.   |  |   |  |  |  |  |  |  |  |  |  |
| 18.   |  | A second copy of the published International Application under 35 U.S.C. 154(d)(4).  |  |   |  |  |  |  |  |  |  |  |  |
| 19.   |  | A second copy of the English language translation of the International application under 35 U.S.C. 154(d)(4).  |  |   |  |  |  |  |  |  |  |  |  |
| 20.   | $\boxtimes$  | Other items or information: Unexecuted Declaration and postcard  |  |   |  |  |  |  |  |  |  |  |  |

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|   |   | 11:30                       | PC                               | T/EP2004/010688   |                |          | 33378A               | JOURLI | NOMBER      |   |  |  |
|---|---|-----------------------------|----------------------------------|---|----------------|----------|----------------------|--------|-------------|---|--|--|
| The following fees are submitted:   |   |                             |                                  |   |                |          | CALCULATIONS PTO USE |        |             |   |  |  |
|   |   |                             |                                  |   |                |          |                      | ONLY   | <u>-</u>    |   |  |  |
| 21. 🛭 Bas   | ic nation   | al fee                      |                                  |   |                |          | \$300                |        |             |   |  |  |
| 22. Examination Fee   |   |                             |                                  |   |                |          |                      |        |             |   |  |  |
| ☐ If International preliminary examination report was prepared by USPTO and all claims satisfy provisions of PCT Article 33(1)-(4)  |   |                             |                                  |   |                |          |                      |        |             |   |  |  |
| •   | . ⊠ All other situations  |                             |                                  |   |                |          |                      |        |             |   |  |  |
| L⊠ All d  | itner situ  | ations                      |                                  | •••••   | • • • •        |          | \$200                |        |             |   |  |  |
| 23. Search fee  |   |                             |                                  |   |                |          |                      |        |             |   |  |  |
| ☐ If Se   | earch fee   | (37 CFR 1.                  | relitited:  fee                  |   |                |          |                      |        |             |   |  |  |
| application to the USPTO as an International Searching Authority\$  |   |                             |                                  |   |                |          |                      |        |             | \$300  \$300  \$\$ \$\$ \$\$ \$\$ \$\$ \$\$ \$\$ \$\$ \$\$ \$\$ \$\$ \$\$ |  |  |
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|   |   |                             |                                  |   |                |          |                      |        |             |   |  |  |
| Additional fee for specification and drawings filed in paper over 100 sheets (excluding sequence listing or computer program listing filed in an electronic medium). The fee is \$250 for each additional 50 sheets of paper or fraction thereof. |   |                             |                                  |   |                |          |                      |        |             |   |  |  |
| Total Sheets  | Extra   | a sheets                    |                                  |   | on             |          | RATE                 | Γ      |             |   |  |  |
| 137 - 100 =   | 37  | /50 -                       | thereof (roun                    | d up to a whole number)                                 |                | V 6      | 050                  |        |             |   |  |  |
|   |   |                             |                                  |   |                | Λ \$     | 250                  | \$     | 250         |   |  |  |
| Surcharge of \$130 for furnishing the oath of declaration later than  |   |                             |                                  |   |                |          |                      |        |             |   |  |  |
| CLAIMS  |   |                             |                                  | NUMBER EXTRA  | _              | R        | ATF                  |        |             |   |  |  |
| Total claims  |   |                             |                                  | 2   | ×              |          |                      | \$     | 100         | <u> </u>  |  |  |
| Independent cla   |   |                             |                                  |   | -              |          |                      |        |             |   |  |  |
| MOLTIPLE DEF  | Elaims 2 -3 = 0 X \$ 200 \$ EPENDENT CLAIM(S) (if applicable) + \$ 360 \$  TOTAL OF ABOVE CALCULATIONS = \$ 1,250 |                             |                                  |   |                |          |                      |        |             |   |  |  |
| Reduction of 1/2 for filing by small entity, if applicable. Verified Small Entity Statement must also be  |   |                             |                                  |   |                |          |                      |        |             |   |  |  |
| filed (Note 37 C  | FR 1.9,   | 1.27, 1.28).                |                                  |   |                |          |                      |        |             |   |  |  |
| Processing fee  | of \$130 f  | for furnishin               | a the English (                  | repolation later than                                   | 20             | SU       | BTOTAL =             | \$     | 1,250       |   |  |  |
| Processing fee of \$130 for furnishing the English translation later than   30 months from the earliest claimed priority date (37 CFR 1.492(f)).  |   |                             |                                  |   |                |          |                      |        |             |   |  |  |
|   | claimed priority date (37 CFR 1.492(f)). + \$  TOTAL NATIONAL FEE = \$ 1,250                                      |                             |                                  |   |                |          |                      |        |             |   |  |  |
| Fee for recording   | ee for recording the enclosed assignment (37 CFR 1.21(h)). The assignment must be accompanied                     |                             |                                  |   |                |          |                      |        |             |   |  |  |
| ру ап арргорпа  | an appropriate cover sheet (37 CFR 3.28, 3.31). \$40 per property + \$  |                             |                                  |   |                |          |                      |        |             |   |  |  |
|   |   |                             | <del></del>                      | TOTAL   |                | LO EN    | CLUSED =             |        |             | <u> </u>  |  |  |
|   |   |                             |                                  |   |                |          |                      |        |             | \$  |  |  |
|   |   |                             |                                  | SUBTOTAL = \$ 1,250  the English translation later than |                |          |                      |        |             |   |  |  |
| a. A chec   | k in the a  | amount of \$                |                                  | to cover the above fe                                   | es is          | enclosed | d.                   |        |             |   |  |  |
| b. 🛛 Please<br>duplica  | charge to   | Deposit Acc<br>of this form | ount No. 19-0<br>is enclosed.    | 134 in the name of Novar                                | tis in         | the amo  | unt of \$1,250 t     | o cove | er the abov | e fees. A   |  |  |
| c. 🛛 The Co   | mmissic   | oner is heret               | by authorized to                 | to charge any additional fe                             | es v           | hich ma  | y be required,       | or cre | dit any ove | erpayment to  |  |  |
|   |   |                             |                                  |   |                |          |                      |        |             |   |  |  |
| NOTE: Where or (b)) must be   | an appro  | opriate time<br>d granted t | e limit under a<br>o restore the | 37 CFR 1.494 or 1.495 ha<br>application to pending      | as no<br>statu | t been r | net, a petition      | to re  | vive (37 C  | FR 1.137(a)   |  |  |
| Send all corresp  | ondence   | e to the add                | ress associate                   | d with  |                | <b>H</b> |                      |        | 1           |   |  |  |
| Customer No. 0  | 01095, w  | hich is curr                | ently:                           |   | 1              | 1/       | 1 1                  | n/     | <u> </u>    |   |  |  |
| Kristin Konzak  |   |                             |                                  |   |                |          |                      |        |             |   |  |  |
| Novartis Attorney for Applicant   |   |                             |                                  |   |                |          |                      | / )    |             |   |  |  |
| Corporate Intellectual Property Reg. No. 44,848   |   |                             |                                  |   |                |          |                      |        |             |   |  |  |
| One Health Plaza, Building 104 (617) 871-3216 East Hanover, NJ 07936-1080   |   |                             |                                  |   |                |          |                      |        |             |   |  |  |
|   |   |                             |                                  |   |                |          |                      |        |             |   |  |  |